REMARKS

This amendment responds to the Office Action mailed on July 15, 2003. In the Office Action, the Examiner rejected claims 47-54 as being indefinite under 35 U.S.C. § 112, first paragraph, claims 47-50 for lack of enablement under 35 U.S.C. § 112, second paragraph and claims 47-54 for obviousness under 35 U.S.C. § 103(a). Claims 47 and 48 have been amended as suggested by the Examiner to clarify the claimed invention. The amendments are fully supported by the instant specification and therefore, are not new matter. (See, *e.g.*, page 51, lines 11-16; page 52, lines 17-19; and page 55, lines 25-27 of the present specification).

The Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 47-54 are rejected under 35 U.S.C. § 112, first paragraph, for alleged failure of the specification to enable a person skilled in the relevant art to make and use the invention commensurate with the scope of the claims. Applicants believe the rejection should be withdrawn for the reasons stated below.

The Examiner alleges that the specification fails to adequately describe the genus of compounds to be used in the methods of the invention. In the instant case, the claimed invention relates to methods of using compounds that inhibit Src kinase activity or HBx mediated activation of the Src kinase signaling cascade in order to inhibit HBV infection (see, *e.g.*, the specification at page 12, lines 24-29). The specification describes a number of compounds that may be used in accordance with the claimed invention, *e.g.*, specific examples of tyrosine kinase or Src kinase inhibitors (see, *e.g.*, the specification at page 27, lines 5-10 and 22-37; at page 28, lines 1-37; at page 18, lines 18-37; and page 19, lines 1-19). The present invention demonstrates that HBx is an intracellular activator of Src kinase and components of the Src signaling cascade (see, Example 6 of the present specification). Consequently, the genus of compounds that may be used in the methods of the invention comprise compounds that inhibit Src kinase activity.

The Examiner contends that the specification does not provide sufficient description of the members of the genus. However, as previously mentioned, the specification does describe members of the genus of compounds that can be used in accordance with the methods of the invention, *e.g.*, a number of specific examples of tyrosine kinase inhibitors. Applicants also point out that the present invention does not claim the compounds

themselves, but rather, a new use for existing compounds and uses of new compounds, having the same or similar properties, *i.e.*, inhibition of enhanced Src kinase activity. The Examiner is respectfully reminded that an applicant is not required to disclose every species that is encompassed by their claims even in an unpredictable art. *In re Angstadt*, 537 F.2d 498 (CCPA 1976). Applicants have disclosed representative examples of known compounds that define members of the genus that can be used in the claimed methods, for example, pyrazolopyrimidine, a selective inhibitor of the Src family of kinases (*see, e.g.*, the specification at page 20, lines 10-15). The specification also provides guidance to distinguish members of the genus. In particular, the specification defines two unifying characteristics of compounds of the invention. First, such compounds are described as Src kinase inhibitors or the Src kinase signal cascade. Second, useful members of the genus are also described as those that inhibit HBV infection. Applicants contend that the specification clearly identifies compounds useful in the claimed methods, and enables one skilled in the art, to identify other compounds that may be used in accordance with the invention. As such, one skilled in the art, provided with the instant specification, would be able to identify members of the genus of compounds that can be used in the claimed methods, without undue experimentation.

Furthermore, the Examiner contends that the specification does not provide guidance to one skilled in the art regarding the types of compounds encompassed by the claimed methods because there is no showing in the specification of the "mechanism" producing inhibition of Src kinase activation induced by HBV and/or HBx. Applicants contend there is no requirement that the mechanism through which the invention works be known. (*see, Exxon Chemical Patents, Inc. v. Lubrizol Corp.* 77 F.3d 450 at 456).

> An inventor need not understand the scientific mechanism in order to place an invention into the patent system. (*see, Newman v. Quigg*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed.Cir.1989) (observing that "it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works"); *Fromson v. AdvanceOffset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed.Cir.1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests.").

Rather, Applicants have shown the viral activities critical to supporting the HBV life cycle, *i.e.*, HBx activation of the Src family of kinases is a critical function provided by HBx for mammalian hepadnavirus replication (*see, e.g.*, page 12, lines 35-37 and page 13, lines 1-2;

and Example 6). One of skill in the art would recognize that HBV replication could be effectively prevented by inhibiting Src kinase activity. Applicants assert that one of skill in the art would be able to identify the types of the compounds encompassed by the claimed invention in light of the specification and without undue experimentation. Therefore, Applicants have enabled the claims under the standard set forth by the Federal Circuit. As such, the pending claims are enabled by the present specification and satisfy the requirements under 35 U.S.C. § 112, first paragraph.

The Examiner's Rejection Under 35 U.S.C. § 112, Second Paragraph Should Be Withdrawn

Claims 47-50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner contends that independent claim 47, from which claims 49-50 depend, is indefinite because one cannot determine the level of Src kinase activity enhancement that results from HBV infection. The Examiner also contends that claim 48 is unclear as to whether the uninfected cell is identical to the infected cell. In response, Applicants have amended the claims as suggested by the Examiner to clarify the claimed invention, therefore obviating the instant rejection. As such, Applicants assert that the rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Cited Art Does Not Render The Pending Claims Obvious

Claims 47-54 are rejected under 35 U.S.C. 103(a) in view of Moriya *et al.* The Examiner contends that it would have been obvious to one of ordinary skill in the art to treat an HBV infected patient or cell with the antisense oligonucleotide of Moriya *et al.* in order to inhibit HBV replication. Applicants believe that the rejection is in error and should be withdrawn for the following reasons.

The present invention is based in part, on Applicants' discovery that activation of cellular Src kinase signaling cascades play a critical role in hepadnavirus replication and that such activation is mediated by HBx. More specifically, the claimed invention relates to a method of inhibiting Hepatitis B virus (HBV) infection or replication comprising administering a compound to an HBV infected patient that inhibits Src kinase activity. In the present instance, the prior art cited by the Examiner does not render obvious the claimed

invention, nor does it provide a reasonable expectation of success that HBV infection can be treated or inhibited using a Src kinase inhibitor. Applicants contend that the cited reference does not provide a proper basis for an obviousness rejection under 35 U.S.C. § 103(a).

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicants' disclosure. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Moriya merely describes the inhibition of expression of a hepatitis B virus gene, *i.e.*, HBx, using an antisense phosphorothioate oligonucleotide. Applicants point out that the cited reference does not suggest a means for inhibiting HBV replication or infection by targeting cellular Src kinase activity, as required by the claimed invention. At best Moriya suggests targeting HBx gene expression via antisense methods, however Moriya does not provide one with a reasonable expectation of success in the treatment or inhibition of HBV infection using the antisense oligo described in Moriya. In fact, Moriya does not even describe the effect of the antisense oligonucleotide on the life cycle or activity of HBV, but rather describes only the effect of the antisense oligonucleotide on HBx gene expression. Furthermore, Moriya only describes one oligonucleotide that was successful in down-regulating HBx gene expression; there is no showing in Moriya that the antisense compound described can prevent HBV infection. Such conclusions are speculative and would hardly provide the necessary reasonable expectation of success required for a finding of obviousness of the claimed invention, which requires targeting cellular kinase activity, not viral gene expression.

The Examiner further contends that the limitation "inhibits Src kinase activity..." merely defines what compounds are being administered by the claimed methods. Applicants point out that the pending claims are directed to methods comprising administering compounds that inhibit Src kinase activity, *i.e.*, claims 47, 48, 51 and 52 expressly relate to methods that use compounds that inhibit Src kinase activity. Nowhere, does Moriya teach or suggest targeting a cellular protein Src kinase to treat HBV infection or replication. At most,

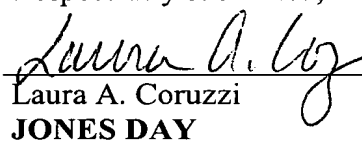
Moriya describes the effect of an antisense molecule on the expression of a viral gene, HBx. In contrast, Applicants respectfully point out that pending independent claims 47, 48, 51 and 52 specifically relate to methods for inhibiting HBV infection using compounds that target cellular kinase activity. Not only does Moriya fail to provide a reasonable expectation of success of inhibiting HBV replication, Moriya does not suggest that one might treat or inhibit HBV replication through the disruption of a cellular kinase activity, which is the crux of Applicants' invention. As such, the cited art fails to provide the required motivation and expectation of success necessary for a finding of obviousness, and the Examiner's rejection of the claims under 35 U.S.C. § 103(a) should be withdrawn.

Conclusion

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of this application. Withdrawal of the Examiner's rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: January 15, 2003



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